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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/538,495	04/13/2006	Gabriella Sozzi	0471-0291PUS1	7078

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EXAMINER	
TUNG, JOYCE	

ART UNIT	PAPER NUMBER
1637	

NOTIFICATION DATE	DELIVERY MODE
03/19/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/538,495	SOZZI, GABRIELLA	
	Examiner	Art Unit	
	Joyce Tung	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,6,7 and 10-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,6,7 and 10-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The response filed 11/16/09 to the Office action has been entered. Claims 1, 3-4, 6-7, 10-14 are pending.

1. The rejections of claims 1, 3-4, and 6-11 under 35 U.S.C. 103(a) over Sozzi et al. (Cancer Research, June 15, 2001, Vol. 61, pg. 4675-4678) in view of Chang et al. (6,664,046, issued Dec. 16, 2003), Cook (7,160,996, issued Jan. 9, 2007), Wick et al. (Gene, 1999, Vol. 232, pg. 97-106), Lowe et al. (Nucleic Acids Research, 1990, Vol. 18(7), pg. 1757-1761) and the attached search report (6,156,504 issued Dec. 5, 2000) are withdrawn because of the arguments filed 11/16/09.

NEW GROUNDS OF REJECTION

Claim Objections

2. Claims 1, and 12 are objected to because of the following informalities: the word "hexonuclease" might be typographic error. Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-4, 6-7, and 10-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The newly added phrase "obtained from a patient who smokes" in claim 1

and step 6 "correlating the hTERT copy number to the risk of cancer in the patient" recited in claim 1 and 12 have no support in the specification. This constitutes new matter.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1, 3-4, 6-7 and 10-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1, 3-4, 6-7 and 10-14 are vague and indefinite because it is unclear what is encompassed by "the risk of cancer in the patient".

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1, 3-4, 7, and 10-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sozzi et al. (Cancer Research, June 15, 2001, Vol. 61, pg. 4675-4678) in view of Cech et al. (6,475789, issued Nov. 5, 2002), Chang et al. (6,664,046, issued Dec. 16, 2003) and Gocke et al. (6,156,504 issued Dec. 5, 2000).

Sozzi et al. disclose circulating DNA quantification with plasma DNA in 84 patients with non-small cell lung cancer. The amount of circulating DNA in plasma could discriminate between lung cancer patients and healthy individuals (see 4675, the Abstract). The sample is a DNA sample extracted from plasma (see pg. 4675, column 2, forth-fifth paragraph). Polymerase chain reaction is performed for quantification (see 4676, column 1, forth paragraph). The data suggest that quantification of plasma DNA in lung cancer patients is a valuable noninvasive diagnostic tool for discriminating from unaffected individuals and for detecting early recurrence during follow-up (See pg. 4675, the Abstract). The circulating plasma DNA is compared with controls (see pg. 4676, table1).

Sozzi et al. do not disclose adding to a target DNA sample: a) a mixture of oligonucleotide primers suitable for PCR amplification of a fragment of the human telomerase reverse transcriptase (hTERT) gene, wherein said fragment of the hTERT gene is from nucleotide position 13059 to nucleotide position 13156 of the sequence of GenBank accession no. AF 128893.

Cech et al. disclose a polynucleotide which encodes hTERT polypeptide (see column 15, lines 1-18) is used as sense or antisense probes or primers for hybridization and/or amplification of naturally occurring hTERT genes for diagnostic or prognostic applications (see column 15, lines 20-28). In one embodiment the gene product is a nucleic acid which is detected by

amplifying the gene and detecting the amplification product where the presence of the complex or amplification product is correlated with the presence of the hTERT gene product in a biological sample (see column 3, lines 44-48). The primers amplify any specific region, for example, coding regions, promoter regions, introns or subsequences of hTERT genomic DNA (see column 16, lines 11-15). hTERT is detected by the primers and probes as disclosed. The method of detection is PCR (see column 81, lines 35-40). The amplified products are directly analyzed by any well known means, for example fluorescent signals (see column 82, lines 32-33).

Cech et al. also indicate that amplification (i.e., change in copy number), deletion (i.e., partial deletion), insertion, substitution, or changes in the chromosomal location (e.g., translocation) of an hTRT gene may be correlated with the presence of a pathological condition or a predisposition to developing a pathological condition (e.g., cancer) (see column 87, lines 66-67 and column 88, lines 1-5).

One of ordinary skill in the art would have been motivated to use the primers and probes as taught by Cech et al. in a DNA extract sample of Sozzi et al. because Cech et al. provide a probe that specially binds to the hTERT gene for amplifying any specific region on the gene (see column 16, lines 11-15). It would have been prima facie obvious to use the oligonucleotide primer as claimed for evaluating a risk of cancer in a smoker,

Sozzi et al. do not disclose b) an oligonucleotide probe, having at least one quencher and one reporter fluorophore at the 3'and 5'ends, able to anneal to a sequence within the region delimited by the primers, in suitable conditions for carrying out a PCR reaction,

3) adding a heat-stable DNA polymerase with 5'-3' hexonuclease activity and amplifying the hTERT gene fragment;

4) measuring the produced fluorescence;

5) quantifying the hTERT DNA copy number in the target DNA sample interpolating a calibration curve created with known amounts of DNA, wherein the concentration of circulating total DNA in a plasma sample is determined by quantification of hTERT copy number.

Chang et al. discuss a probe-based method for quantifying amplified products (see column 9, lines 27-64). The teachings of Chang et al. read on steps 3) and 4). Quantitation of a sample containing an unknown number of target sequences typically is carried out with reference to a "standard curve" generated from a series of amplifications of samples containing a target sequence in a range of known amounts (See column 10, lines 14-18). The teachings of Chang et al. read on the limitations as set forth above.

One of ordinary skill in the art would have been motivated to use the quantification method as discussed by Chang to quantify hTERT DNA copy number because methods of quantification of amplified products were well known in the art. It would have been prima facie obvious to carry out these steps as claimed.

None of the references discloses a plasma specimen obtained from a smoker.

Gocke et al. disclose a method for screening both healthy individuals, and individuals at risk for cancer and premalignant conditions (See column 8, lines 59-61) including lung cancer from smokers (See column 30, lines 63-67).

One of ordinary skill in the art would have been motivated to apply the method of Sozzi et al. for the evaluation of the risk of cancer development in smokers because the method of Gocke et al. discloses detecting the presence of extracellular DNA in blood plasma via DNA amplification for the detection, monitoring, or evaluation of cancer or premalignant conditions (See column 3, lines 66-67 and column 4, lines 1-7) including lung cancer from smokers (See column 30, lines 63-67). It would have been prima facie obvious to carry out evaluation of the risk of cancer development in smokers as claimed.

8. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sozzi et al. (Cancer Research, June 15, 2001, Vol. 61, pg. 4675-4678) in view of Cech et al. (6,475789, issued Nov. 5, 2002), Chang et al. (6,664,046, issued Dec. 16, 2003) and Gocke et al. (6,156,504 issued Dec. 5, 2000) as applied to claims 1, 3-4, 7, and 10-14 above, and further in view of Wick et al. (Gene, 1999, Vol. 232, pg. 97-106), Lowe et al. (Nucleic Acids Research, 1990, Vol. 18(7), pg. 1757-1761) and the attached sequence search report.

The teachings of Sozzi et al, Cech et al., Chang et al., and Gocke et al. are set forth in section 7 above. None of the references discloses SEQ ID NO: 1-3 used as primers and a probe for amplifying the fragment of hTERT gene.

Wick et al. disclose the complete genomic organization of the hTERT gene and isolated the 5'- and 3' flanking region. The hTERT gene encompasses more than 37kb and consists of 16 exons. These results provide the basis for more detailed studies on the regulation of telomerase activity in normal and cancer cells and may lead to the development of new cancer therapies (See pg. 97, the Abstract). As indicated in the search sequence report, the nucleic acid sequence of the hTERT gene comprises SEQ ID NO: 1-3 (See the attached search report).

As indicated in the nucleic acid sequence search report, SEQ ID NO: 6 disclosed by Cech et al. which is an hTERT genomic clone comprises instant SEQ ID NOs: 1 and 3 (see the attached nucleic acid sequence search report) used in the instant method as a primer and probe recited in claim 6.

Lowe et al. disclose criteria for primer selection from known nucleotide sequences (see pg. 1758, column 1).

One of ordinary skill in the art would have been motivated to design primers and probes from a known nucleic acid sequence, for example, the nucleic acid of hTERT gene as disclosed by Wick et al. for amplifying the fragment of the hTERT because Lowe et al. disclose criteria for routine primer selection (see pg. 1758, column 1). It would have been prima facie obvious to use SEQ ID NO: 1-3 as primers and probes for amplifying a fragment of hTERT gene.

Summary

9. No claims are allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (571) 272-0790. The examiner can normally be reached on Monday - Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kenneth R Horlick/
Primary Examiner, Art Unit 1637

/Joyce Tung/
Examiner, Art Unit 1637
March 4, 2010